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REMARKS/ARGUMENTS

Reconsideration of the application in view of the above amendments and following remarks is requested. Claims 33-36 are now in the case. Claim 33 has been amended. No new matter has been added.

Applicants reserve the right to prosecute claims to canceled subject matter in one or more continuing applications.

Claim 33 has been amended to recite an antibody that specifically binds to an epitope of a polypeptide consisting of a sequence of amino acid residues as shown in SEQ ID NO:2 from residue 235 to residue 345, wherein said antibody is a monoclonal antibody or a single-chain antibody. Support for amended claim 33 is found within the specification as filed, such as at pages 54, 55, and elsewhere. Production of monoclonal and single-chain antibodies with the recited specificity is neither taught nor suggested by Ferrara et al., taken either alone or in combination with Ladner et al. Hence, the amended claims are believed to be patentable over the art of record.

Claims 33, 34, and 36 stand rejected under 35 USC 102(e) as allegedly anticipated by Ferrara et al., U.S. Patent No. 6,391,311 B1. The Office maintains that, given Ferrara's teaching, one would obtain antibodies within the metes and bounds of the claims.

Applicants believe that this rejection is overcome by the amendment of claim 33. Monoclonal antibodies are highly specific antibodies that are produced by hybridomas, which are cloned to produce "monoclonal" cell lines. The resulting cell line secretes a single antibody (i.e., a single specificity). Thus, a monoclonal antibody is prepared free from other antibodies (although it can later be combined with other monoclonal antibodies to produce a mixture). See, Academic Press Dictionary of Science and Technology, Academic Press, 1992 ("a homogeneous antibody that is produced by a clone of antibody-forming cells and that binds with a single antigenic determinant"). Ferrara does not direct one skilled in the art to the recited region of VEGF-E and therefore does not teach or suggest the recited monoclonal antibodies. Reconsideration and withdrawal of the rejection under 35 USC 102(e) are requested.

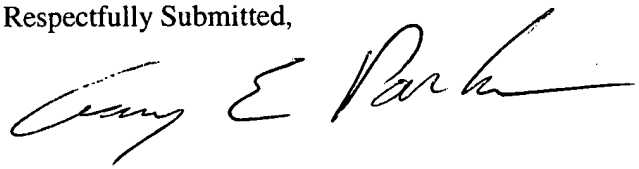
Claim 35 stands rejected under 35 USC 103(a) over Ferrara et al. in view of Ladner et al. (U.S. Patent No. 4,946,778) for reasons of record.

Applicants respectfully traverse this ground of rejection. Single-chain antibodies are genetically engineered antibody fragments with a defined specificity. Ladner et al. teaches that "heavy and light (H and L) polypeptide chains from the variable region of a given antibody" are converted into a single polypeptide chain by the application of a computer-based method of selecting linkers (column 7, lines 8-16; emphasis added). See also, column 29, lines 63-65 ("The specificity of the antibody to

be engineered will be determined by the original selection process."). Thus, as taught by Ladner et al., one must first select an antibody of a certain specificity. The resulting single-chain antibody will be free from other antibodies. Neither Ferrara et al. nor Ladner et al. teaches the selection of an antibody that specifically binds to an epitope of a polypeptide consisting of a sequence of amino acid residues as shown in SEQ ID NO:2 from residue 235 to residue 345. Claim 35 is therefore patentable over the combined references. Reconsideration and withdrawal of the rejection under 35 USC 103(a) are requested.

Applicants believe that each rejection has been addressed and overcome. Reconsideration of the application and its allowance are requested. If for any reason the Examiner feels that a telephone conference would expedite prosecution of the application, the Examiner is invited to telephone the undersigned at (206) 442-6673.

Respectfully Submitted,



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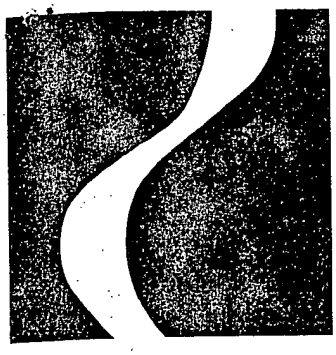

Academic Press Dictionary of Science and Technology

Edited by
Christopher Morris

Academic Press
Harcourt Brace Jovanovich, Publishers
San Diego New York Boston London Sydney Tokyo Toronto

Academic Press, Inc.
1250 Sixth Avenue, San Diego, California 92101-4311

United Kingdom Edition published by
Academic Press Limited
24–28 Oval Road, London NW1 7DX

Library of Congress Cataloging-in-Publication Data

Academic Press dictionary of science and technology / edited by
Christopher Morris
p. cm.
ISBN 0-12-200400-0
1. Science--Dictionaries. 2. Technology--Dictionaries.
I. Morris, Christopher G. II. Academic Press. III. Title:
Dictionary of science and technology.
Q123.A33 1991
503--dc20 90-29032
CIP

PRINTED IN THE UNITED STATES OF AMERICA
92 93 94 95 96 97 DO 9 8 7 6 5 4 3 2 1

...*Vertebrate Zoology.* any of several bottom-dwelling sharks of ...*Squatina*, family Squatinidae, characterized by large, lateral, ...ectoral and ventral fins; found in tropical and warm temperate ...

...al *Vertebrate Zoology.* a member of any of three endangered ...s small, dark brown seals belonging to the genus *Monachus*: ...chus of the Mediterranean, *M. tropicalis* of the Caribbean, or ...insland*i* of the Hawaiian Islands.

...hood *Botany.* a plant, *Aconitum napellus*, of the family Ranun... whose flowers have a large, hood-shaped sepal.

...combining form meaning "one" or "single." *Chemistry.* specif... combining form indicating: **1.** the presence of a single atom, ... radical, etc. **2.** uniformity or similarity of composition, size, ... properties, etc.

...cetate *Organic Chemistry.* a compound that contains one ac... group, such as an ester or a salt.

...cetin see ACETIN.

...cid *Chemistry.* an acid containing only a single replaceable hy... atom. Thus, **monoacidic.** Also, MONACID.

...delic *Genetics.* of a polyploid individual, having identical alleles ...given locus.

...mine *Organic Chemistry.* any amine containing only one amino ... g., serotonin, dopamine, or norepinephrine.

...mine oxidase *Enzymology.* the flavin-containing amine oxi... important in the catabolism of epinephrine and tyramine.

...mine oxidase inhibitor *Pharmacology.* any of a group of an... ...ive drugs that block the oxidative deamination of monoamines.

...minergic *Neurology.* of or relating to neurons that secrete ...line neurotransmitters.

...mic *Chemistry.* of a molecule, consisting of a single atom. ...NATOMIC.

...tomic gas *Chemistry.* any gas composed of single atoms.

...sic *Chemistry.* of an acid, having one replaceable hydrogen ...per molecule.

...sic calcium phosphate *Inorganic Chemistry.* $Ca(H_2PO_4)_2$ ...olorless triclinic crystals; soluble in water and acids; loses its ... its melting point of 109°C and decomposes at 203°C; used in ...powders, fertilizers, and mineral supplements, and as a plastic ... Also, CALCIUM BIPHOSPHATE, PRIMARY CALCIUM PHOSPHATE.

basic magnesium phosphate *Inorganic Chemistry.* $(PO_4)_2 \cdot 2H_2O$, a white, crystalline, hygroscopic powder that is sol... water and acids and insoluble in alcohol; decomposes on heat... in plastics and fireproofing.

basic sodium phosphate *Inorganic Chemistry.* NaH_2PO_4, a ...rystalline powder, or the hydrated form $NaH_2PO_4 \cdot H_2O$, white ...both very soluble in water; used in dyeing, electroplating, acid ...baking powders, and for many other purposes.

...thrida *Paleontology.* an order of camerate crinoids; generally ...ean; Lower Ordovician to Upper Permian.

...yte *Histology.* an immature monocyte, usually found in the ...row and spleen.

...tic leukemia see ACUTE MONOCYTIC LEUKEMIA.

...toma *Oncology.* a tumor containing monoblasts and mono...

...pharidaceae *Mycology.* a family of microscopic fungi of the ...noblepharidales living in soil and water and on organic mate... as fruit and twigs.

...pharidales *Mycology.* an order of fungi of the class Chytrid... found in aquatic habitats as nonparasites that live on dead ...ter.

...projectile *Ordnance.* an armor-piercing projectile consist... ...e piece of heat-treated steel; it may have a false ogive.

...circuit *Electronics.* an integrated circuit in which multiple ...integrated circuit chips are interconnected or interwired with ...components, to form a larger single-package circuit.

...*Mechanical Engineering.* an aerial ropeway in which a sin... ...rope is used to both support and move loads.

...*Botany.* describing a plant that fruits once and then dies.

...ous *Botany.* describing a plant having a single carpel or ...

...*Genetics.* of a chromosome, having only one centromere.

...idae *Vertebrate Zoology.* the pinecone fishes, a mono... ...family of Indo-Pacific fish of the order Beryciformes, character... ...or ctenoid scales, large eyes, and luminous organs under

Monoceros *Astronomy.* the Unicorn, a large but faint constellation straddling the celestial equator just east of Orion.

Monoceros Loop *Astronomy.* a supernova remnant about 50,000 years old that lies in the galactic plane northeast of the Rosette Nebula in Monoceros.

Monoceros R2 molecular cloud *Astronomy.* a large, active star-forming region in Monoceros.

monocharge electret *Electronics.* a foil electret that has electrical charges of the same sign on both surfaces.

monochasium *Botany.* a cyme with a main axis producing a single lateral branch.

monochlamydous *Botany.* describing plants whose perianth has only a single whorl.

monochromat *Medicine.* a person affected by monochromatism.

monochromatic [män´ō krə mat´ik] *Optics.* **1.** relating to or describing one color or hue. **2.** relating to or describing electromagnetic radiation with one wavelength or with a narrow range of wavelengths. *Medicine.* relating to or affected by monochromatism. *Microbiology.* referring to staining with only one dye at a time.

monochromatic filter see BIREFRINGENT FILTER.

monochromatic interference *Optics.* the interference of two or more beams of light of the same wavelength.

monochromatic neutron beam *Nucleonics.* a beam of neutrons in which the energy values are extremely limited.

monochromatic radiation *Electromagnetism.* electromagnetic radiation of an extremely narrow band.

monochromatic temperature scale *Thermodynamics.* a temperature scale that is defined according to the amount of power radiated by a blackbody at a particular wavelength.

monochromatism *Medicine.* complete color blindness, in which all colors of the spectrum appear as neutral grays with varying shades of light and dark. Also, MONOCHROMIA.

monochromator *Optics.* a source of monochromatic light characterized by thin entrance and exit slits that control the spectral width of emitted light, a prism, and additional lenses and mirrors to control the path of the light.

monochrome [män´i krōm´] *Optics.* relating to or describing different shades of the same color, such as gradations of black.

monochrome channel *Electronics.* in a color television system, the path for carrying the monochrome signal.

monochrome signal *Electronics.* a signal wave in television transmission that controls the luminance values in the picture, but not the chromaticity values.

monochrome television see BLACK-AND-WHITE TELEVISION.

monochromophilic *Microbiology.* stainable by only one kind of stain.

monocistronic *Molecular Biology.* describing a mRNA molecule that encodes the information necessary for synthesis of a single polypeptide chain.

Monocleaceae *Botany.* a monogeneric family of liverworts characterized by plants with dichotomous branching, a thallus without differentiation of midrib, epidermal pores or photosynthetic air chambers, and a large gametophyte.

Monocleales *Botany.* the single, monogeneric order of liverworts of the order Marchantiidae, characterized by a gametophyte that is one of the largest among the liverworts.

monoclimax *Ecology.* a type of climax community in which there is only one controlling factor, especially a climatic factor.

monoclimax theory *Ecology.* the theory that over time and within a climatic region, there will be a single regional climax community.

monoclinal *Geology.* of, relating to, or being a monocline.

monocline *Geology.* a portion of a stratigraphic sequence that is not part of an anticline or syncline, but dips from the horizontal in one direction.

monoclinic system *Crystallography.* a unit cell in which there is a two-fold rotation axis parallel to one cell axis (usually chosen as *b*); as a result there are no restrictions on the axial ratios, but the angles made by *b* with *a*, and *b* with *c*, must be 90° ($\alpha = \gamma = 90°$). Also, **monoclinic unit cell.**

monoclinous *Botany.* describing a flower that is a hermaphrodite, having both stamens and pistils. Thus, **monoclinism.**

monoclonal *Biology.* referring to a substance that is derived from a single clone or family of cells; derived from a single cell.

monoclonal antibody *Biotechnology.* a homogeneous antibody that is produced by a clone of antibody-forming cells and that binds with a single antigenic determinant.